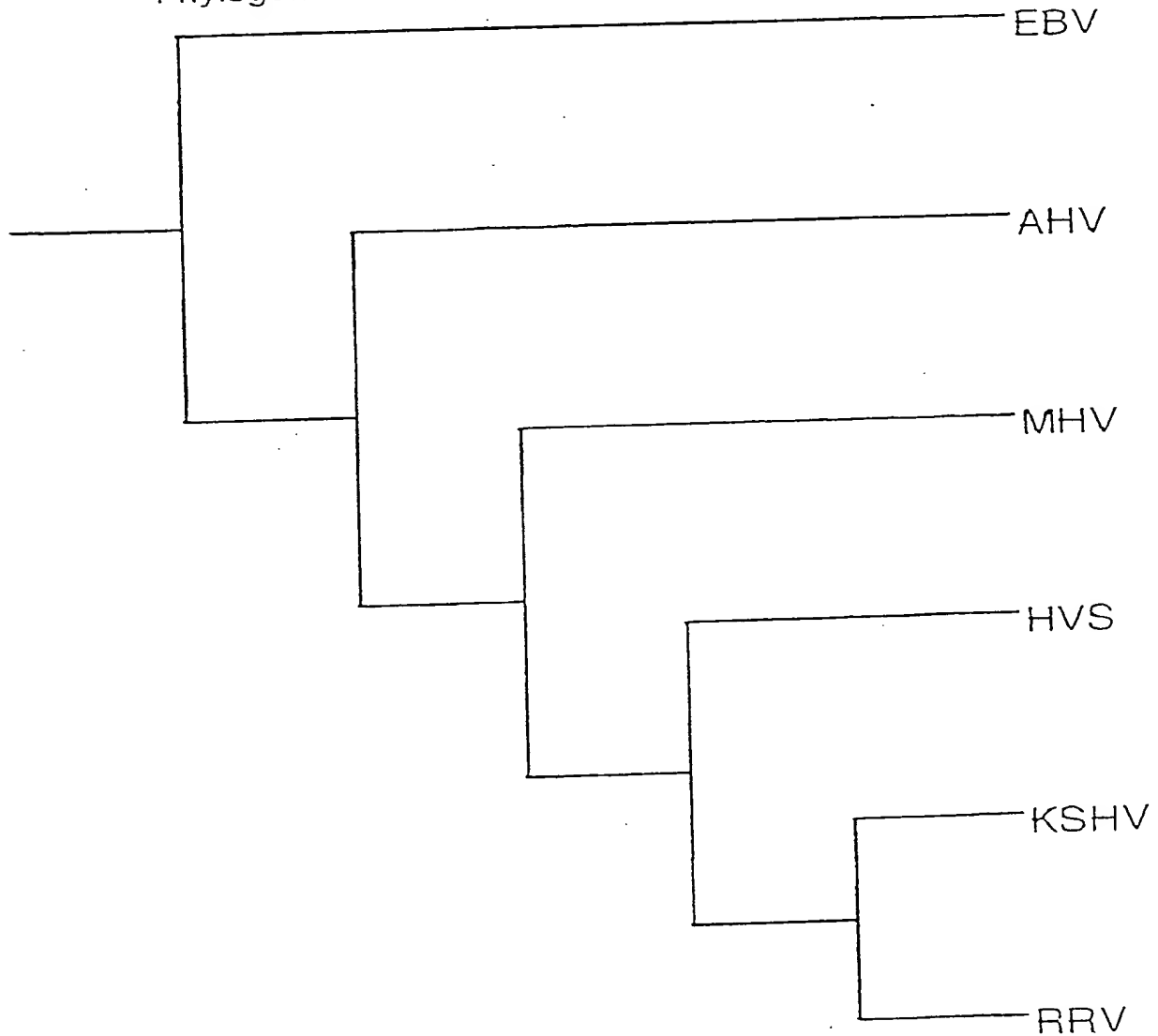


**FIG. 1**

## Phylogenetic Comparison of the Gammaherpesviruses



EBV - Epstein-Barr virus  
AHV - Alcelaphine herpesvirus  
MHV - Murine herpesvirus 68  
HVS - Herpesvirus saimiri  
KSHV - Kaposi's sarcoma-associated herpesvirus  
RRV - Rhesus rhadinovirus 17577

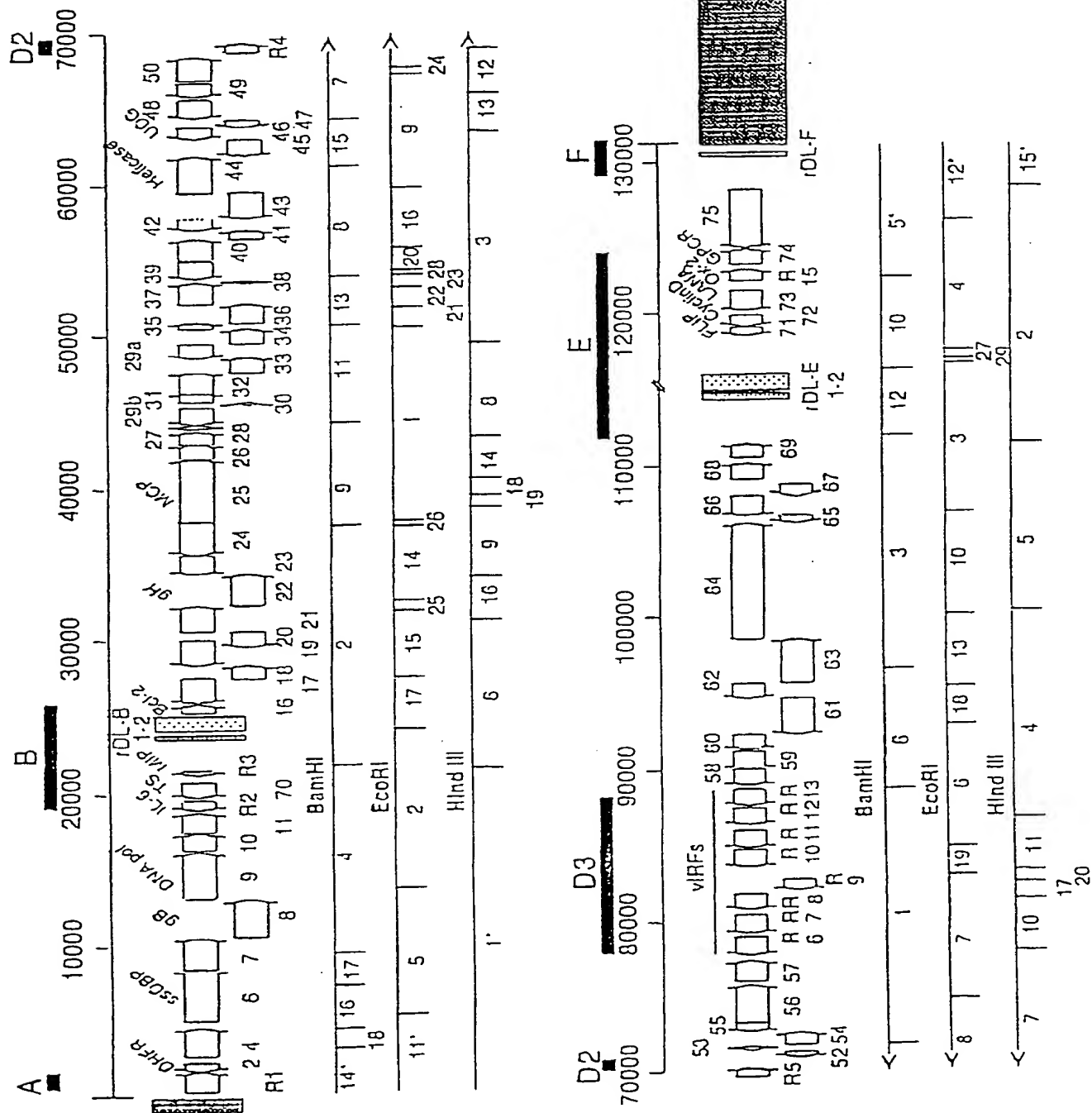
FIG. 2

## Restriction Fragments of the RRV 17577 Genome

BamHI		EcoRI		Hind III	
fragment number	fragment size (bp)	fragment number	fragment size (bp)	fragment number	fragment size (bp)
1	17189	1	12476	1*	22006
2	15598	2	10342	2	17108
3	15441	3	9565	3	16542
4	12360	4	9213	4	14134
5*	8943	5	8465	5	11516
6	7747	6	8036	6	10743
7	7718	7	7969	7	8452
8	7142	8	7416	8	5995
9	6667	9	7278	9	4679
10	6474	10	7002	10	3374
11	6333	11*	5400	11	2963
12	3978	12*	5054	12	2891
13	3411	13	4907	13	2849
14*	3157	14	4771	14*	2832
15	3008	15	4272	15	1599
16	2916	16	4099	16	1272
17	2210	17	3516	17	1016
18	1343	18	2102	18	853
		19	1858	19	811
		20	1603		
		21	1512		
		22	1221		
		23	910		
		24	624		
		25	609		
		26	592		
		27	584		
		28	122		
		29	107		

\* Indicates that the fragment size excludes terminal repeat sequences

FIG. 3



WO 00/28040

4/13

PCT/US99/26260

## FIG. 4

MacVector Output for long unique region of rhesus  
rhadinovirus 17577

LOCUS 4 LONG UNIQUE 131634 BP DS-DNA

UPDATED 06/26/98

DEFINITION -

ACCESSION -

KEYWORDS -

SOURCE -

FEATURES

## Description

pept

1 R1

pept

(C1 Similar to HHV8 Orf 2 - dihydrofolate reductase

pept

1 Similar to HHV8 Orf 4 - complement binding  
protein

pept

1 Similar to HHV8 Orf 6 - ssDNA binding protein

pept

1 Similar to HHV8 Orf 7 - transport protein

pept

1 Similar to HHV8 Orf 8 - glycoprotein B

pept

1 Similar to HHV8 Orf 9 - DNA polymerase

pept

1 Similar to HHV8 Orf 10

pept

1 Similar to HHV8 Orf 11

pept

(C1 R2 viral II-6

pept

(C1 Similar to HHV8 Orf 70

pept

(C1 R3 similar to HHV8 MIP ..

frag

(C) misc. feature MIP homology, but no initiation  
codon

rpt

repeat sequence

rpt

repeat sequence

pept

1 Similar to HHV8 Orf 16 - Bcl-2 homolog

pept

(C1 Similar to HHV8 Orf 17 - capsid protein

pept

1 Similar to HHV8 Orf 18

pept

(C1 Similar to HHV8 Orf 19 - tegument protein

pept

(C1 Similar to HHV8 Orf 20

pept

1 Similar to HHV8 Orf 21 - thymidine kinase

pept

1 Similar to HHV8 Orf 22 - glycoprotein H

pept

(C1 Similar to HHV8 Orf 23

pept

(C1 Similar to HHV8 Orf 24

pept

1 Similar to HHV8 Orf 25 - major capsid protein

pept

1 Similar to HHV8 Orf 26 - capsid protein

pept

1 Similar to HHV8 Orf 27

pept

1 Similar to HHV8 Orf 28

pept

(C1 Similar to HHV8 Orf 29b

pept

1 Similar to HHV8 Orf 30

pept

1 Similar to HHV8 Orf 31

pept

1 Similar to HHV8 Orf 32

pept

1 Similar to HHV8 Orf 33

pept

(C1 Similar to HHV8 Orf 29a

pept

1 Similar to HHV8 Orf 34

pept

1 Similar to HHV8 Orf 35

pept

1 Similar to HHV8 Orf 36 - kinase

pept

1 Similar to HHV8 Orf 37 - alkaline exonuclease

pept

1 Similar to HHV8 Orf 38

pept

(C1 Similar to HHV8 Orf 39 - glycoprotein H

pept

1 Similar to HHV8 Orf 40 - helicase - primase

pept

1 Similar to HHV8 Orf 41 - helicase - primase

pept

(C1 Similar to HHV8 Orf 42

pept

(C1 Similar to HHV8 Orf 43 - capsid protein

pept

1 Similar to HHV8 Orf 44 - helicase - primase

pept

(C1 Similar to HHV8 Orf 45

FIG. 5

Comparison of Corresponding Repeats in  
RRV and KSHV

virus	insert name	total length	repeat unit length	G + C content
KSHV	<i>frnk</i> <sup>1</sup>	332 bp 292 bp	20 bp 30 bp	80.1% 84.9%
RRV	<i>syko</i> <sup>1</sup>	304 bp 1008 bp	26 bp 25 bp	53.3% 79.9%
KSHV	<i>zppa</i> <sup>1</sup>	308 bp 244 bp	23 bp 23 bp	74.0% 77.9%
RRV	<i>vrigo</i> <sup>1</sup>	405 bp 1029 bp	19 bp 32 bp	74.6% 84.4%
virus	insert name	total length	repeat unit length	G + A content
KSHV	<i>mdsk</i>	409 bp	— <sup>2</sup>	75.4%
RRV	<i>brds</i>	196	13 bp	81.6%

<sup>1</sup> KSHV *frnk* and *zppa* and RRV *syko* and *vrigo* are tandem repeats.

<sup>2</sup> KSHV *mdsk* is a complex repeat with no defined unit length.

FIG. 6

Comparison of Interferon regulatory elements coded by RRV and KSHV<sup>a</sup>

	KSHV K9	KSHV K10	KSHV K10.1	KSHV K10.5	KSHV K11	Rh R6	Rh R7	Rh R8	Rh R9	Rh R10	Rh R11	Rh R12	Rh R13
KSHV K9	100.000 100.000	100.000 100.000				26.044 21.130	20.291 20.728	20.857 19.427		33.705 26.184	29.972 21.849		
KSHV K10	100.000 100.000	100.000 100.000											
KSHV K10.1	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	32.036 21.895								
KSHV K10.5	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000								
KSHV K11	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000		26.393 19.062	29.918 22.131	54.427 47.917			
Rh R6	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	34.513 26.254			50.773 41.495	33.038 24.484	
Rh R7	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000		31.412 24.207	35.693 23.849	61.254 50.997	20.018 21.037
Rh R8	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	20.900 18.367	20.216 21.577	30.364 18.623	50.103 52.964
Rh R9	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	32.951 23.496	33.526 25.723	
Rh R10	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	33.923 23.849	31.124 25.072
Rh R11	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	
Rh R12	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000
Rh R13	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000	100.000 100.000

<sup>a</sup> Blank cells indicated no similarity; upper number is percent similarity; lower number is percent identity.

WO 00/28040

7/13

**FIG. 7A**  
Comparison of RRV, KSHV and HVS ORFs

ORF	Strand	Size aa	KSHV			HVS			Putative Function
			Size aa	% Sim	% I	Size aa	% S	% I	
R11	+	423							
Orf 2	-	188							
Orf 42	+	645	210 550	55.1% 40.9%	46.0% 35.7%	187 360	65.6% 42.0%	54.8% 35.3%	Dihydrofolate reductase Complement binding protein
Orf 6	+	1132	1133	71.3%	63.3%	287	44.0%	38.6%	ssDNA binding protein
Orf 7	+	686	695	60.1%	51.5%	1128	65.2%	53.5%	Transport protein
Orf 8	+	829	845	73.3%	65.5%	808	62.4%	53.1%	Glycoprotein B
Orf 9	+	1014	1312	75.0%	67.0%	1009	71.0%	62.5%	DNA polymerase
Orf 10	+	384	418	43.5%	34.8%	407	33.6%	23.3%	
Orf 11	+	409	407	41.3%	31.7%	405	46.3%	32.4%	
R21	-	207							
Orf 70	-	333	337	72.1%	66.1%	294	72.1%	64.6%	Thymidylate synthase
R33	-	115	95	41.9%	32.3%				
Orf 16	+	187	175	58.0%	46.0%	160	31.4%	21.4%	Bcl-2 homolog
Orf 17	-	536	553	50.6%	44.3%	475	49.0%	42.2%	Capsid protein
Orf 18	+	299	257	68.1%	58.0%	256	60.2%	48.8%	
Orf 19	-	547	549	61.1%	52.8%	543	55.5%	46.9%	Tegument protein
Orf 20	-	350	320	51.8%	44.7%	303	43.2%	35.6%	
Orf 21	+	557	580	54.0%	44.6%	527	39.0%	31.7%	Thymidine kinase
Orf 22	+	704	730	50.1%	40.7%	717	42.3%	31.5%	Glycoprotein H
Orf 23	-	402	404	56.8%	48.5%	253	40.5%	29.8%	
Orf 24	-	732	752	66.3%	58.7%	731	56.3%	46.8%	
Orf 25	+	1378	1376	79.9%	72.5%	1371	76.7%	67.5%	Major capsid protein
Orf 26	+	307	305	71.8%	64.3%	304	69.1%	58.2%	Capsid protein
Orf 27	+	269	290	33.6%	25.3%	280	35.0%	27.1%	
Orf 28	+	91	102	30.1%	26.5%	93			
Orf 29b	-	348	351	77.6%	66.4%	387	74.4%	62.9%	Packaging protein
Orf 30	+	76	77	51.3%	38.2%	75	40.3%	29.2%	
Orf 31	+	217	224	56.0%	45.4%	208	50.5%	39.9%	

FIG. 7B

RRV			KSHV			HVS			Putative Function
ORF	Strand	Size aa	Size aa	% Sim	% I	Size aa	% S	% I	
Orf 32	+	464	454	49.9%	41.8%	441	43.2%	34.1%	Packaging protein
Orf 33	+	336	312	52.1%	42.1%	330	49.1%	39.1%	
Orf 29a	-	327	312	66.7%	61.2%	303	57.8%	49.8%	
Orf 34	+	327	327	58.9%	48.5%	316	53.7%	40.6%	
Orf 35	+	149	151	47.7%	35.6%	150	51.0%	37.4%	Kinase
Orf 36	+	435	444	56.0%	46.1%	431	38.4%	28.7%	
Orf 37	+	480	486	72.4%	63.5%	483	63.0%	53.2%	Alkaline exonuclease
Orf 38	+	69	61	56.7%	45.0%	66	39.4%	34.8%	
Orf 39	-	378	399	73.0%	59.3%	366	67.1%	57.0%	Glycoprotein M
Orf 40	+	468	457	42.2%	32.7%	450	39.1%	28.1%	
Orf 41	+	203	205	33.5%	26.0%	161	37.3%	29.1%	Helicase-primase
Orf 42	-	272	278	56.8%	46.1%	265	51.2%	38.1%	
Orf 43	-	576	605	69.7%	61.6%	563	66.4%	56.6%	Capsid protein
Orf 44	+	790	788	73.9%	66.0%	781	71.1%	62.6%	
Orf 45	-	352	407	31.2%	24.9%	257			Helicase-primase
Orf 46	-	255	255	71.9%	60.1%	252	67.5%	59.1%	
Orf 47	-	169	167	31.9%	27.7%	141	33.3%	23.9%	Uracyl DNA glucosidase
Orf 48	-	389	402	36.2%	29.2%	797	34.1%	25.8%	
Orf 49	-	301	302	66.1%	54.2%	303	35.1%	23.3%	Glycoprotein L
Orf 50	+	514	631	46.6%	37.8%	535	29.7%	21.6%	
R41	+	206							Transactivator
R51	+	111							
Orf 52	-	139	131	58.5%	45.4%	115	41.7%	30.4%	dUTPase
Orf 53	-	104	110	51.0%	46.2%	90	43.3%	28.9%	
Orf 54	+	290	318	48.6%	41.0%	287	46.5%	36.4%	
Orf 55	-	210	227	62.9%	55.2%	200	52.5%	44.4%	
Orf 56	+	828	843	61.2%	52.5%	835	54.0%	43.6%	DNA replication protein
Orf 57	+	442	275	60.6%	47.1%	416	40.3%	31.5%	
R64	-	415		26.0%	21.1%				Immediate-early protein
R74	-	415		28.3%	20.7%				
R84	-	351		28.9%	19.4%				



FIG. 7C

ORF	RRV		KSHV		HVS		Putative Function
	Strand	Size aa	Size aa	% Sim	Size aa	% S	
R94	-	253					
R104	-	385		33.7%			
R114	-	390		30.0%			
R124	-	355					
R134	-	364					
Orf 58	-	360	357	45.2%	357	39.9%	DNA replication protein
Orf 59	-	394	396	60.3%	368	40.7%	Ribonucleotide reductase, small
Orf 60	-	314	305	78.2%	305	71.0%	Ribonucleotide reductase, large
Orf 61	-	788	792	69.3%	767	64.4%	Ribonucleotide reductase, large
Orf 62	-	331	331	64.4%	330	53.8%	Assembly / DNA maturation
Orf 63	+	939	927	51.8%	899	43.4%	Tegument protein
Orf 64	+	2548	2635	49.6%	2469	39.2%	Tegument protein
Orf 65	-	169	170	48.2%	139	41.0%	Capsid protein
Orf 66	-	448	429	51.9%	435	43.6%	
Orf 67	-	224	271	69.6%	253	58.6%	Tegument protein
Orf 68	+	457	545	53.2%	436	53.5%	Glycoprotein
Orf 69	+	297	225	73.1%	261	57.5%	
R141	-	228					
Orf 71	-	174	139	38.8%	167	25.3%	Flip homolog
Orf 72	-	254	257	49.8%	254	37.5%	Cyclin D homolog
Orf 73	-	447	1162	23.6%	407	29.0%	Immediate-early gene
R155	+	253	348	35.2%			
Orf 74	+	342	342	51.6%	321	41.1%	G-protein coupled receptor
Orf 75	-	1298	1296	52.2%	1299	43.2%	Tegument protein / FGARAT

% Sim., percent similar; % Id., percent identical; ssDNA, single-stranded DNA; FGARAT, N-formalglycinamide ribotide amidotransferase; 1, no similarity found; 2, compared to HVS ORF 4a and 4b; 3, compared to KSHV R4; 4, compared to KSHV K9; 5, compared to KSHV K14.

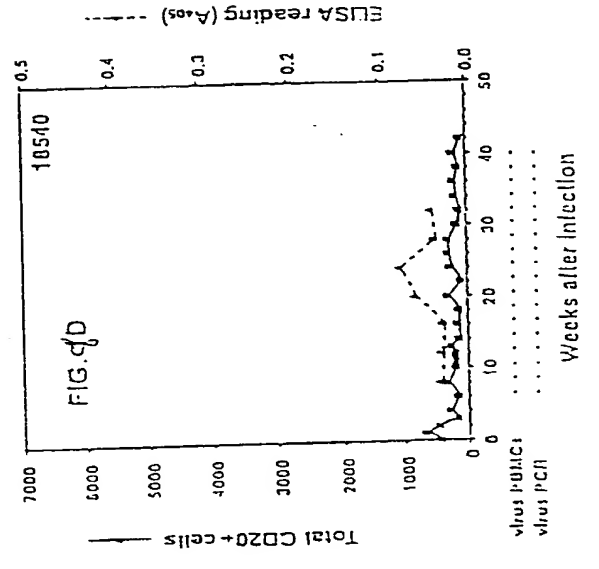
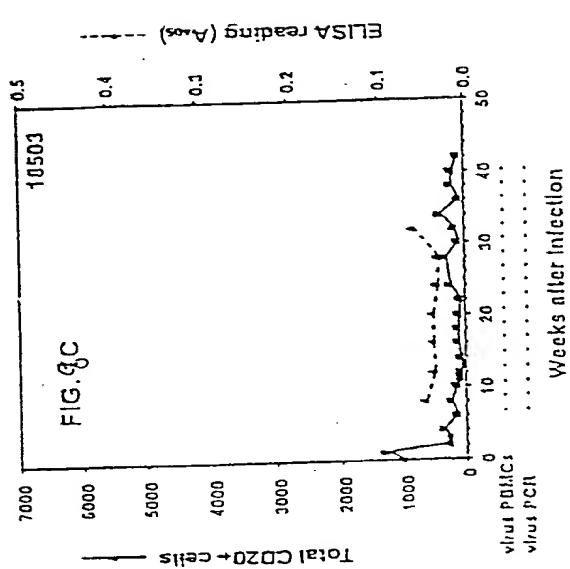
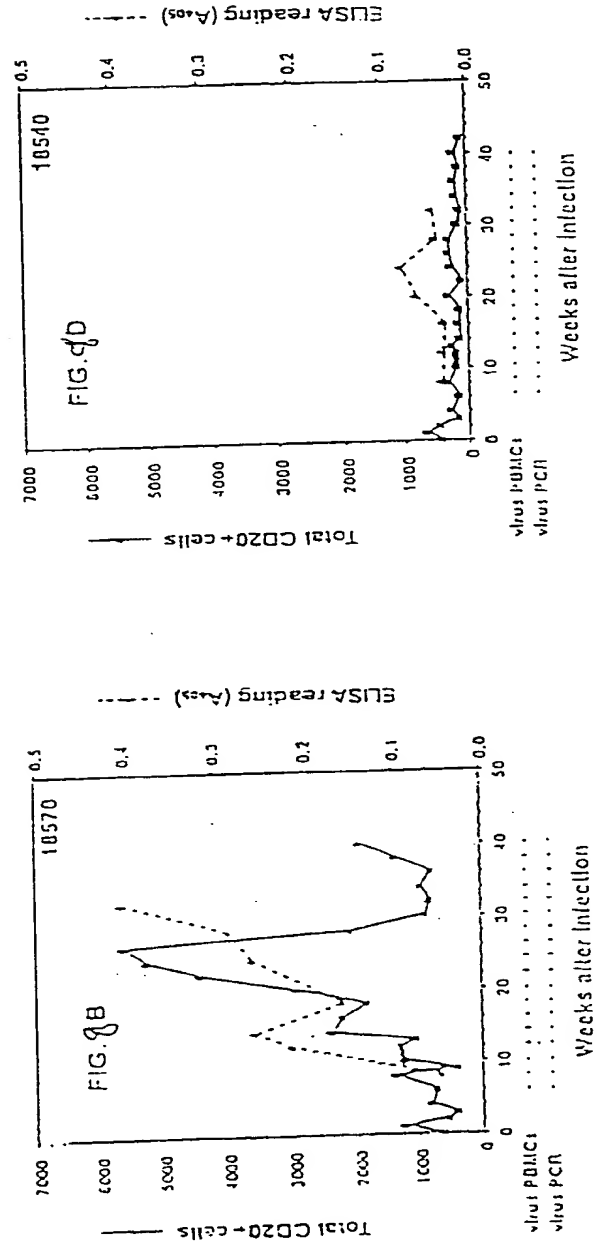
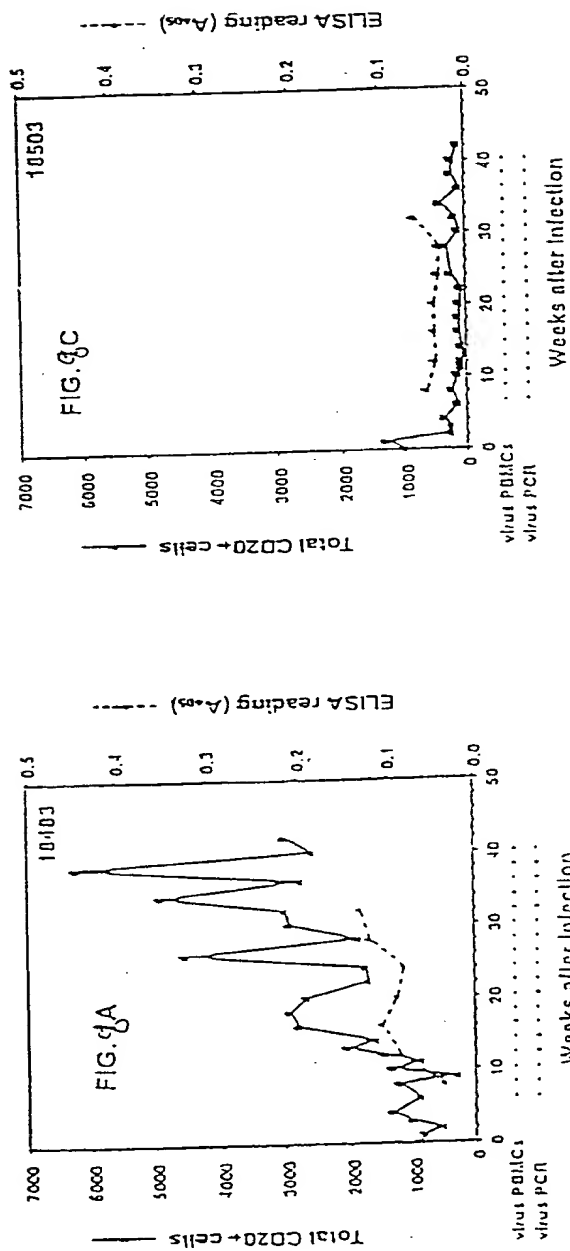


FIG. 8

11/13

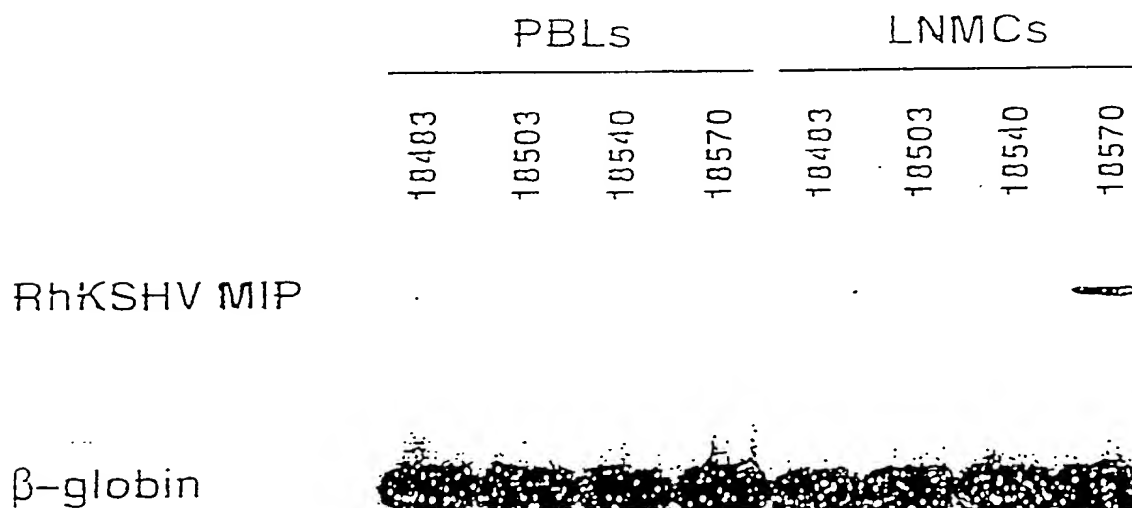
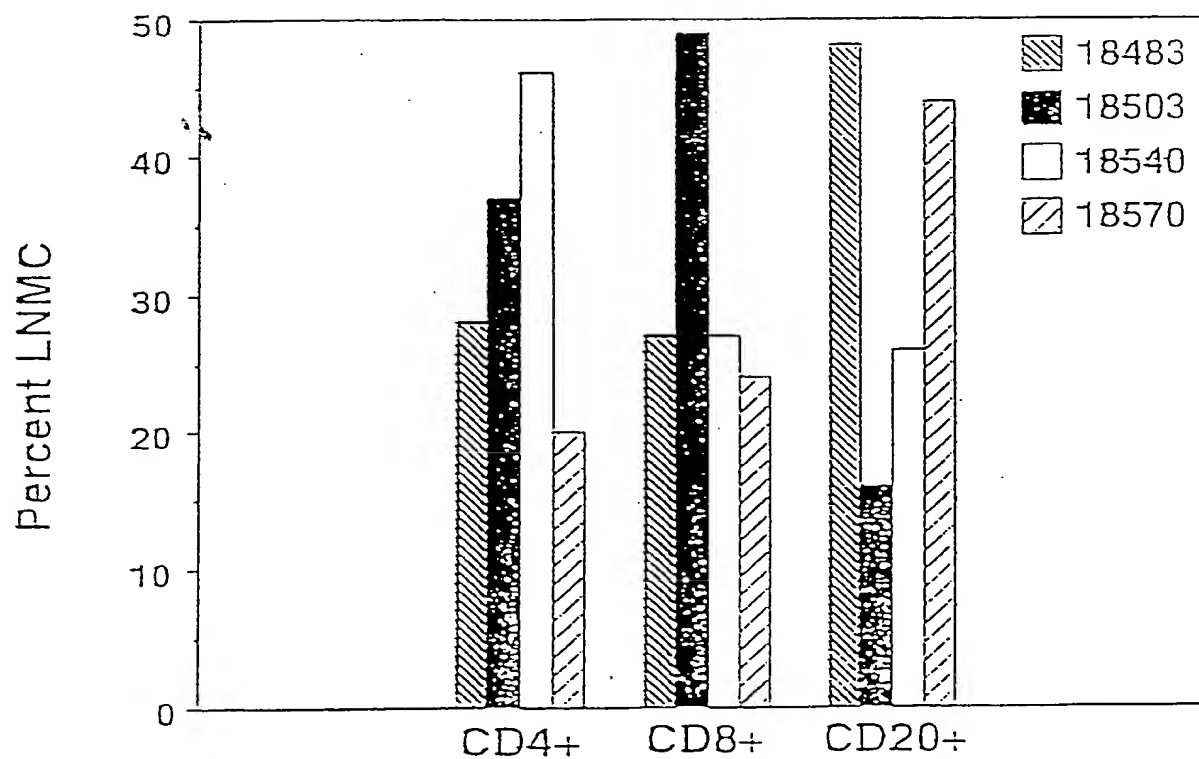


FIG. 9

12/13

FIG. 10

atg ttc cct gtc tgg ttc gtc ttg ttt tac ctg tct tgt tgg gcg gcc	48
Met Phe Pro Val Trp Phe Val Leu Phe Tyr Leu Ser Cys Trp Ala Ala	
1 5 10 15	
agc cct acg ctg gcg cct ccc ccg act gcc gct gga att aac gtt ctc	96
Ser Pro Thr Leu Ala Pro Pro Pro Thr Ala Ala Gly Ile Asn Val Leu	
20 25 30	
ccc cag tgg gcc ggc aac cgc gcc tct ctt gac agg acc agg ggg cgc	144
Pro Gln Trp Ala Gly Asn Arg Ala Ser Leu Asp Arg Thr Arg Gly Arg	
35 40 45	
ctg tct gaa gtg ggg tta aac ata cag cgc tgg ttc gtt tac ctg tgc	192
Leu Ser Glu Val Gly Leu Asn Ile Gln Arg Trp Phe Val Tyr Leu Cys	
50 55 60	
cac cac tcc act ctc tgt cgg gtg cgt gag tac ccg cgc atc atg tct	240
His His Ser Thr Leu Cys Arg Val Arg Glu Tyr Pro Arg Ile Met Ser	
65 70 75 80	
ttt gtt cac ttc cct ata ttg atg tct aac gtt gag tgc cag cgc cgc	288
Phe Val His Phe Pro Ile Leu Met Ser Asn Val Glu Cys Gln Arg Arg	
85 90 95	
gag ttt cgc ggg gcc gag tgt atg aac gcc atg gtt cgc ggg ctc cgg	336
Glu Phe Arg Gly Ala Glu Cys Met Asn Ala Met Val Arg Gly Leu Arg	
100 105 110	
gcc tac gag agt tac ctg acg cga ctg agg atg ctg ctg gac gac gcg	384
Ala Tyr Glu Ser Tyr Leu Thr Arg Leu Arg Met Leu Leu Asp Asp Ala	
115 120 125	
ccc ggg gac gcg gac gcc gcg gcc att ggc tcc gcg gtg acc gtg gtg	432
Pro Gly Asp Ala Asp Ala Ala Ile Gly Ser Ala Val Thr Val Val	
130 135 140	
ctg tcc gcc ctc gac tct cta att gag gag ctt ccc gta aat aac aag	480
Leu Ser Ala Leu Asp Ser Leu Ile Glu Glu Leu Pro Val Asn Asn Lys	
145 150 155 160	
ata ggt ggc gcg gag tct aat gaa aaa acc gtg cgt gcg ttg gga ggg	528
Ile Gly Gly Ala Glu Ser Asn Glu Lys Thr Val Arg Ala Leu Gly Gly	
165 170 175	
cag agc ccc cgg gac gtt gtt ctc agc gcg ttt cgc ata ctg gaa tat	576
Gln Ser Pro Arg Asp Val Val Leu Ser Ala Phe Arg Ile Leu Glu Tyr	
180 185 190	
cta cag atg ttt ttg cgg gac ggg cgc cgc gca ata gct atg atg taa	624
Leu Gln Met Phe Leu Arg Asp Gly Arg Arg Ala Ile Ala Met Met	
195 200 205	

## FIG. 11

atg agg ggc ctt ttc gtg tgc gtt ttt ttt gcg gtg ttc gcg tgt gta	48
Met Arg Gly Leu Phe Val Cys Val Phe Phe Ala Val Phe Ala Cys Val	
1 5 10 15	
gtt gat tat gcc ttt cct atg ggc tcc atg agc gga ccc gcg ccc gaa	96
Val Asp Tyr Ala Phe Pro Met Gly Ser Met Ser Gly Pro Ala Pro Glu	
20 25 30	
ctc tgc tgt ttg ggg tat gta act cat ctg ccg cca ccc ggt tta gtg	144
Leu Cys Cys Leu Gly Tyr Val Thr His Leu Pro Pro Pro Gly Leu Val	
35 40 45	
gtc tct tac tcc cac acc tcg tcg cag tgc tcg gtg gac gcc gtg ata	192
Val Ser Tyr Ser His Thr Ser Ser Gln Cys Ser Val Asp Ala Val Ile	
50 55 60	
tta aac act cgc cgc ggt aaa aag ctg tgt gcc aat ccc ggg gac gac	240
Leu Asn Thr Arg Arg Gly Lys Lys Leu Cys Ala Asn Pro Gly Asp Asp	
65 70 75 80	
gca gtg aag aaa ctg ctt cag gcg gtg gac aag cgt ccc aaa aag ggc	288
Ala Val Lys Lys Leu Leu Gln Ala Val Asp Lys Arg Pro Lys Lys Gly	
85 90 95	
aga aga acc cgg cgc agc ctg att gac gat tcc gaa gag ggc ctt ggc	336
Arg Arg Thr Arg Arg Ser Leu Ile Asp Asp Ser Glu Glu Gly Leu Gly	
100 105 110	
agc ggg att tag	348
Ser Gly Ile	
115	